

PCT/IB2005/000204

Attorney Docket No. 060348/0119

WHAT IS CLAIMED IS:

1. A composition comprising (i) intact minicells that contain a small molecule drug and (ii) a pharmaceutically acceptable carrier therefor.
2. The composition of claim 1, wherein said composition contains fewer
5 than about 1 contaminating parent bacterial cell per 10^7 minicells.
3. The composition of claim 1, wherein said composition contains fewer than about 1 contaminating parent bacterial cell per 10^8 minicells
4. The composition of claim 1, wherein said composition contains fewer than about 1 contaminating parent bacterial cell per 10^9 minicells
- 10 5. The composition of claim 1, wherein said composition contains fewer than about 1 contaminating parent bacterial cell per 10^{10} minicells
6. The composition of claim 1, wherein said composition contains fewer than about 1 contaminating parent bacterial cell per 10^{11} minicells.
7. A composition consisting essentially of intact minicells that contain a
15 small molecule drug.
8. A targeted drug delivery method that comprises bringing bispecific ligands into contact with (a) bacterially derived minicells that contain a small molecule drug and (b) target mammalian cells, such that (i) said bispecific ligands cause said minicells to bind to said mammalian cells, (ii) said minicells are engulfed
20 by said mammalian cells, and (iii) said small molecule drug is released into the cytoplasm of said mammalian cells.
9. The method of claim 8, wherein said target mammalian cells are non-phagocytic cells.
10. The method of claim 8, wherein said bispecific ligand comprises
25 polypeptide or carbohydrate or glycopeptide.

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11. The method of claim 8, wherein said bispecific ligand comprises a first arm that carries specificity for a bacterially derived minicell surface structure and a second arm that carries specificity for a non-phagocytic mammalian cell surface receptor.
- 5 12. The method of claim 11, wherein said first arm and said second arm are monospecific.
13. The method of claim 11, wherein said first arm and said second arm are multivalent.
14. The method of claim 11, wherein said minicell surface structure is an
10 O-polysaccharide component of a lipopolysaccharide on said minicell surface.
15. The method of claim 11, wherein said minicell surface structure is a member of the group consisting of outer membrane proteins, pilli, fimbrae, flagella, and cell-surface exposed carbohydrates.
16. The method of claim 11, wherein said mammalian cell surface receptor
15 is capable of activating receptor-mediated endocytosis of said minicell.
17. The method of claim 8, wherein said bispecific ligand comprises an antibody or antibody fragment.
18. The method of claim 8, wherein said bispecific ligand comprises a humanized antibody.
- 20 19. The method of claim 8, wherein said minicell comprises an intact cell wall.
20. The method of claim 8, wherein said small molecule drug is a chemotherapeutic agent.
21. The method of claim 8, wherein said mammalian cells are *in vitro*.
- 25 22. The method of claim 8, wherein said mammalian cells are *in vivo*.

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23. A drug delivery method that comprises bringing bacterially derived minicells that contain a small molecule drug into contact with mammalian cells that are phagocytosis- or endocytosis-competent, such that said minicells are engulfed by said mammalian cells and said small molecule drug is released into the cytoplasm of said mammalian cells.
24. The method of claim 23, wherein said minicells comprise an intact cell wall.
25. The method of claim 23, wherein said small molecule drug is a chemotherapeutic agent.
26. The method of claim 23, wherein said minicells are *in vitro*.
27. The method of claim 23, wherein said minicells are *in vivo*.
28. A method of loading minicells with a drug, comprising the step of creating a concentration gradient of said drug between an extracellular medium containing said minicells and the minicell cytoplasm, such that said drug moves down said concentration gradient, into the minicell cytoplasm.
29. A composition comprising (i) a bacterially derived minicell that contains a small molecule drug molecule and (ii) a bispecific ligand that is capable of binding to a surface component of said minicell and to a surface component of a non-phagocytic mammalian cell.
30. Use of bacterially derived intact minicells and bispecific ligands in the preparation of a medicament, said minicells containing a small molecule drug and said bispecific ligands being capable of binding to said minicells and to target non-phagocytic mammalian cells, for use in a method of treating a disease or modifying a trait by administration of said medicament to a cell, tissue, or organ.